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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,243	02/05/2001	Yoram Kapulnik	01/21632	2822

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EXAMINER
KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
1638	20

DATE MAILED: 08/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/762,243	KAPULNIK ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this c mmunicati n appears on the cover sheet with the c rresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-51* is/are pending in the application.

4a) Of the above claim(s) *3, 5, 8, 15-17, 23, 30, 34 and 39-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6,7,9-14,18-22,24-29,31-33,35-38,50 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 May 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 52-53 have been cancelled, claims 1-2, 7, 9-11, 13-14, 18-19, 22, 24-26, 28, 21, 33, 35-36, 38 and 50 have been amended, the substitute specification has been entered, and the specification has been amended as requested in Paper No. 19, field 27 May 2003.

2. This application contains claims 3, 5, 8, 15-17, 23, 30, 34 and 39-49 drawn to inventions nonelected without traverse in Paper No. 13. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01. Claims 1-2, 4, 6-7, 9-14, 18-22, 24-29, 31-33, 35-38 and 50-51 are examined.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the U.S. Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

Response to Amendment

5. The objection to claims 1, 7, 13-14, 18, 22, 24, 26, 28, 33, 38 and 53 because of informalities is WITHDRAWN in light of amendments to the claims.

Claim Rejections - 35 USC § 112

6. Claims 1-2, 4, 5-7, 9-14, 18-22, 24-29, 31-33, 35-38 and 50-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Neither the instant specification nor the originally filed claims appear to provide support for the phrase "vegetative plant tissue". The specification states that the invention is drawn to a method of effecting degeneration of somatic plant tissue (pg 2, lines 12-13), and "somatic" is defined as referring to both vegetative and reproductive plant tissues, not either vegetative or reproductive plant tissues (pg 25, lines 10-13).

Thus, such a phrase constitutes NEW MATTER. In response to this rejection, Applicant is required to point to support for the phrase or to cancel the new matter.

7. Claims 1-2, 4, 6-7, 9-14, 18-22, 24-29, 31-33, 35-38 and 50-51 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for streptavidin-encoding constructs with the αβ gliadin storage protein signal sequence for secretion and the streptavidin processing sequences, and with and without the bacterial streptavidin signal peptide, expressed from a constitutive promoter, methods of using them to transform plants, and plants so

obtained, does not reasonably provide enablement for constructs encoding an biotin-binding protein, including derivatives of biotin and streptavidin, proteins without a secretion signal sequence or streptavidin with the processing sequences, methods of using them to transform plants, plants so obtained, or methods of plastid transformation with a construct encoding a biotin-binding protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is repeated for the reasons of record as set forth in the Office action mailed 4 December 2002, as applied to claims 1-2, 4, 6-7, 9-14, 18-22, 24-29, 31-33, 35-38 and 50-53. Applicant's arguments filed 27 May 2003 have been fully considered but they are not persuasive.

Applicant urges that although the instant application provides a limited number of examples, these illustrate that selective somatic plant tissue degeneration can be efficiently utilized to control plant morphology. Applicant urges that the specification provides the guidance to generate and employ expression constructs that use other biotin depleting proteins. Applicant cites a PCT application that putatively describes proteins that deplete essential factors. Applicant cites a website to state that modified streptavidin can be purchased commercially, cites Akeshi et al, which describes streptavidin variants, and cites Gitlin et al (1990, Biochem. J. 269:527-530), which describes the biotin binding site. Applicant cites Watanabe et al (1998) and Van Wuytswinkel et al (1998, Plant J. 17:93-97), stating that they describe proteins that deplete essential factors. Applicant thus urges that numerous examples of essential factor binding proteins are available, and that unnamed publications outline methodology for generation of derivatives/modificants (response pg 8-10).

This is not found persuasive. Gitlin et al teach inactivation of avidin and streptavidin; as the instant method requires functional "derivatives" and "modificants", Gitlin et al fails to provide enablement for such proteins. The transgenic plants produced by Van Wuytswinkel et al did not have degeneration of vegetative tissue of the plant, even though they were made using all the same steps provided in the instant claims; thus, Van Wuytswinkel et al fail to provide enablement for the instant specification. The website, the PCT application, Watanabe et al (1998) and Akeshi et al could not considered because they were not sent.

Watanabe et al (2001, Physiol. Plant. 112:546-55) was sent, but was published after the filing date of the instant application. See *In re Glass*, 181 USPQ 31, 34 (CCPA 1974), which teaches that references published after the filing date of an application may not be relied upon for the enablement of the specification.

Applicant urges that one of ordinary skill in the art would be capable of identifying and generating sequences encoding essential factor binding proteins and derivatives/modificants thereof and publications outlining methodology are available (response pg 10-11).

This is not found persuasive. This is an unsupported assertion only, and such publications were not sent. Furthermore, making all possible single amino acid substitutions in an 128 amino acid long protein like avidin would require making and analyzing 19^{128} nucleic acids and making all possible single amino acid substitutions in an 184 amino acid long protein like streptavidin would require making and analyzing 19^{184} nucleic acids. thus, without guidance making "modificants" is not straightforward.

Applicant urges that the specification teaches that use of a signal sequence is not essential to depletion of essential factors, and that targeting to organelles can be replaced with organelle

transformation. Applicant cites Koop et al (1996, Planta 199:193-201), Zoubenko et al (1994, Nuc. Acids Res. 22:38-19-3824), and Svab et al to state that organelle transformation was known at the time of filing. Applicant urges that Binder et al (1996, Plant Mol. Biol. 32:303-314) teaches plant specific promoters (response pg 11).

This is not found persuasive. Koop et al and Zoubenko et al only teach transformation of tobacco plastids, and do not teach transformation of the plastids of other plants or mitochondrial transformation. Binder et al may teach mitochondrial promoters, but does not teach mitochondrial transformation. Svab et al could not considered because it was not sent. The claims should be written to state that the protein is expressed either using a signal sequence or expressed within a tobacco plastid, if there is support within the specification.

Applicant urges that although plants expressing streptavidin without the described signal sequence dies at the seedling or embryo stage, one could use a weaker or inducible promoter to produce the desired effect, and such strategies are described in the specification (response pg 11-12).

This is not found persuasive because Applicant did not cite the pages at which such strategies are described. The summary on pg 25-27of promoters usable in the invention do not discuss "weak" promoters. The root specific Tob promoter used to express streptavidin without a signal sequence is inducible because it is induced by signals within the cell. Thus, use of a weaker or inducible promoter is not enabled.

8. Claims 1-2, 4, 6-7, 9-14, 18-22, 24-29, 31-33, 35-38 and 50-51 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 4 December 2002, as applied to claims 1-2, 4, 6-7, 9-14, 18-22, 24-29, 31-33, 35-38 and 50-53. Applicant's arguments filed 27 May 2003 have been fully considered but they are not persuasive.

Applicant urges that the specification provides the guidance to generate and employ expression constructs that use other biotin depleting proteins. Applicant cites a PCT application that putatively describes proteins that deplete essential factors. Applicant cites a website to state that modified streptavidin can be purchased commercially, cites Akeshi et al, which describes streptavidin variants, and cites Gitlin et al (1990, Biochem. J. 269:527-530), which describes the biotin binding site. Applicant cites Watanabe et al (1998) and Van Wuytswinkel et al (1998, Plant J. 17:93-97), stating that they describe proteins that deplete essential factors. Applicant thus urges that numerous examples of essential factor binding proteins are available, and that unnamed publications outline methodology for generation of derivatives/modificants (response pg 8-10).

This is not found persuasive. Gitlin et al teach inactivation of avidin and streptavidin; as the instant method requires functional "derivatives" and "modificants", Gitlin et al fails to provide description for such proteins. The transgenic plants produced by Van Wuytswinkel et al did not have degeneration of vegetative tissue of the plant, even though they were made using all the same steps provided in the instant claims; thus, Van Wuytswinkel et al fail to provide description for the instant specification. The website, the PCT application, Watanabe et al (1998) and Akeshi et al could not considered because they were not sent.

Written description requires both a functional and structural description. "Depleting essential factors" is vague and fails to provide the required functional description of the protein - depleting essential factors is not its normal function in cell.

Applicant urges that one of ordinary skill in the art would be capable of identifying and generating sequences encoding essential factor binding proteins and derivatives/modificants thereof and publications outlining methodology are available (response pg 10-11).

This is not found persuasive. Such publications were not sent. The structural features that describe these derivatives/"modificants" are not provided.

9. Claims 2, 7, 19, 22, 31 and 33 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is modified from the rejection set forth in the Office action mailed 4 December 2002, as applied to claims 1-2, 4, 6-7, 9-14, 18-22, 24-29, 31-33, 35-38 and 50-53, due to amendment of the claims. Applicant's arguments filed 27 May 2003 have been fully considered but they are not persuasive.

Claims 7, 22 and 33 are indefinite in their recitation of "biotin binding derivatives" and "modificants thereof".

Applicant urges that http://complex.fiz.huji.ac.il/~mult2020/froy.html modificant uses in to describe a variant, which is well-known term in the art that differs from a derivative in that unlike a derivative it does not include a portion of the native molecule but simply included variants in the sequence (response pg 12).

This is not found persuasive because a copy of the website was not sent. However, from Applicant's description, it does not appear to define "modificant" as not including a portion of the native molecule but simply includes "variants" in the sequence. Wouldn't variants have a portion of the native molecule, or do variants have to have all the nucleic acids or amino acids changed? And if so, what are they changed to?

The following rejections are new, due to amendment, or were not addressed in the response:

Parts (i) to (v) of claims 2 and 19 do not make sense as criteria for selection of the "manner" of expression of a heterologous protein in a plant. It is not clear, for example, how the level of expression of a heterologous protein can be used to determine the "manner" in which the protein is expressed. It is not clear, for example, what the level of expression is - is this the desired level in the transformed plant? The level of the protein in its native source? Something else entirely?

Claim 7 lacks antecedent basis for the limitation "The transgenic plant of claim 6" as claim 6 is drawn to a method.

Claim 31 is indefinite in its recitation of "plant virus derived promoter". As parent claim 28 refers to a plant promoter, how can the promoter be derived from a virus?

Claim Rejections - 35 USC § 102

As Applicant discusses all three rejections together, they will be discussed together here, after recitation of the rejections.

10. Claims 1-2, 4, 6-7, 9, 13-14, 18-22, 24, 28-29, 31-33, 38 and 50 remain rejected under 35 U.S.C. 102(b) as being anticipated by Howard et al (WO 96/40949). The rejection is repeated for the reasons of record as set forth in the Office action mailed 4 December 2002. Applicant's arguments filed 27 May 2003 have been fully considered but they are not persuasive.

11. Claims 1-2, 4, 6-7, 9, 12-14, 18-22, 24, 27-29, 31-33, 37-38 and 50 remain rejected under 35 U.S.C. 102(b) as being anticipated by Baszczynski et al (1998, US Patent 5,767,379). The rejection is repeated for the reasons of record as set forth in the Office action mailed 4 December 2002, as applied to claims 1-2, 4, 6-7, 9, 12-14, 18-22, 24, 27-29, 31-33, 37-38, 50 and 52. Applicant's arguments filed 27 May 2003 have been fully considered but they are not persuasive.

12. Claims 1-2, 4, 6-7, 9, 12-14, 18-22, 24, 27-29, 31-33, 37-38 and 50 remain rejected under 35 U.S.C. 102(e) as being anticipated by Albertson et al (US Patent 5,962,769, filed July 1997). The rejection is repeated for the reasons of record as set forth in the Office action mailed 4 December 2002, as applied to claims 1-2, 4, 6-7, 9, 12-14, 18-22, 24, 27-29, 31-33, 37-38, 50 and 52-53. Applicant's arguments filed 27 May 2003 have been fully considered but they are not persuasive.

Applicant urges that the amendment to recite vegetative tissue instead of somatic tissue distinguishes the instant invention over the prior art (response pg 13).

This is not found persuasive because each of the references teaches expression of a sequence encoding a biotin-binding protein from the constitutive ubiquitin promoter. The constitutive ubiquitin promoter causes expression in all, or almost all plant tissues, and would thus cause expression of the protein in vegetative tissue.

Claim Rejections - 35 USC § 103

As Applicant discusses both rejections together, they will be discussed together here, after recitation of the rejections.

13. Claims 1-2, 4, 6-7, 9-14, 18-22, 24-29, 31-33, 36-38 and 50-51 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Baszczynski et al (1998, US Patent 5,767,379 in view of Mariani et al (1997, US Patent 5,689,041). The rejection is repeated for the reasons of record as set forth in the Office action mailed 4 December 2002, as applied to claims 1-2, 4, 6-7, 9-14, 18-22, 24-29, 31-33, 36-38 and 50-53. Applicant's arguments filed 27 May 2003 have been fully considered but they are not persuasive.

14. Claims 1-2, 4, 6-7, 9-10, 12-14, 18-22, 24-25, 27-29, 31-33, 35, 37-38 and 50 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Baszczynski et al (1998, US Patent 5,767,379 in view of Maliga et al (1996, US Patent 5,530,191). The rejection is repeated for the reasons of record as set forth in the Office action mailed 4 December 2002, as applied to claims 1-2, 4, 6-7, 9-10, 12-14, 18-22, 24-25, 27-29, 31-33, 35, 37-38, 50 and 52. Applicant's arguments filed 27 May 2003 have been fully considered but they are not persuasive.

Applicant is of the opinion that the references do not render the instant invention obvious, and one of ordinary skill in the art would not be motivated to combine the teachings. Applicant urges that Mariani et al and Maliga et al describe degeneration using a protease or DNase that is toxic to plant cells and whose effects cannot be readily reversed, and the plants produced are sterile. Applicant urges that none of the references described the use for anything other than producing sterile plants (response pg 13-14).

This is not found persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., degeneration that is not toxic to plant cells and whose effects cannot be readily reversed and non-sterile plants) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Conclusion

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
August 5, 2003

AMY J. NELSON, PH.D
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